

Application No.:

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recites “[l]inker arms may include alkylene groups of 1 to 12 carbon atoms, alkenylene groups of 2 to 12 carbon atoms and 1 or 2 olefinic bonds, alkynylene groups of 2 to 12 carbon atoms and 1 or 2 acetylenic bonds, or such groups substituted at a terminal point with nucleophilic groups such as oxy, thio, amino or chemically blocked derivatives thereof...”

Claims 21 and 22 are directed to compounds having a pyrimidine base moiety and modified as noted above for the pyrazolo[3,4-d]pyrimidines (see, for example, Schemes 1 and 2, columns 7 and 8). The specification at column 7, lines 22-40, notes that the invention is directed to two classes of compounds that have demonstrated particular usefulness upon incorporation into oligonucleotides. The first class of compounds are the pyrimidine derivatives, the preparation of which is shown in Schemes 1 and 2. A comparison of the side chain components finds that these schemes illustrate the incorporation of alkynylene, alkenylene and alkylene chains which terminate in Y', a group useful for the attachment of A'. Accordingly, Applicants have added claims 21 and 22 directed to these intermediates, but reducing the scope in view of, for example, Robins et al., Can. J. Chem. 60:554 (1982) and J. Org. Chem. 48:1854 (1983), and Ward et al., U.S. Pat. No. 4,711,955 references of record in the parent application.

Claims 23-28 are directed to oligonucleotides incorporating the modified bases provided in claims 16-22. Support for these claims can be found in those areas provided above for the nucleotide units and in the statement beginning at column 7, line 22, that “[t]wo classes of modified 2’deoxynucleosides have demonstrated particular usefulness in the present invention *for incorporation into oligonucleotides ...*” (emphasis added).

New claims 29-30 and 31-32 are dependent on claims 10 and 13, respectively and recite the limitations wherein the reporter group is selected from  $^3\text{H}$ ,  $^{125}\text{I}$ ,  $^{35}\text{S}$ ,  $^{14}\text{C}$  and  $^{32}\text{P}$  (see column 14, lines 1-4), and more preferably,  $^3\text{H}$ .

New claims 33-44 are directed to the compounds and oligonucleotides having bases and labels as provided above, but having linking groups including the unsaturated linking groups (e.g., alkenylene and alkynylene). More particularly, claim 33 recites a labeled oligonucleotide having at least one pyrazolo[3,4-d]pyrimidine nucleotide unit with a reporter group (A) attached via a linker (W). Support for this group of embodiments can be found at column 9, lines 28-60, wherein W is a chemical linker arm (see column 9, line 51, and column

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10, lines 33-35) and A is a reporter group (see column 9, lines 53-55). The portion designated in the specification as  $-(X)_n-$  is not depicted in the claimed formula as the subscript n is 0 in this group of embodiments. Claims 34 and 35 recites certain radiolabels (see column 14, lines 1-4).

In a related group of embodiments, claims 36-38 recite similar labeled oligonucleotides in which the label is pendent to a pyrimidine base, e.g., as depicted in column 7. In order to be consistent with claims 33-35, the pendent linker and label have been depicted as -W-A, in which W and A have the same definitions as provided above. Applicants believe the equivalent scope sought for linking group and reporter group in this series of claims would be apparent to one of skill in the art upon viewing the general structure, Schemes 1 and 2, and the recitation that two classes of modified bases have demonstrated usefulness in the present invention.

Claims 39-41 and 42-44 recite groups of compounds (pyrazolo[3,4-d]pyrimidines and pyrimidines, respectively) having attached reporter groups. More particularly, these claims are directed to the monomers used in the oligonucleotides provided in claims 33-38. Support in the specification can be found as outlined above.

Applicants believe no new matter is presented in any portion of the requested amendments.

Concerning the sequence listings contained in the specification, the Office's attention is respectfully directed to the enclosed Cross-Reference under 37 C.F.R. § 1.821(e); and Statement under 37 C.F.R. §§ 1.821 (f) and (g).

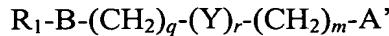
#### CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.



WHAT IS CLAIMED IS:

1                   1. (Amended) An oligonucleotide having at least one nucleotide of  
2                   the formula



4                   wherein

5                   R<sub>1</sub> is a 1-( $\beta$ -D-ribofuranosyl) or 1-( $\beta$ -D-2-deoxyribofuranosyl) group which is  
6                   optionally substituted on one or more of its hydroxyl functions with a Z group,  
7                   wherein Z independently is methyl or a phosphate, thiophosphate, alkylphosphate  
8                   or alkanephosphonate group;

9                   B is a heterocyclic base selected from purine and pyrazolo[3,4-d]pyrimidine groups  
10                  wherein the (CH<sub>2</sub>)<sub>q</sub> group is attached to the 7-position or 8 position of the purine  
11                  and 3-position of the pyrazolo[3,4-d]pyrimidine groups and the R<sub>1</sub> group is  
12                  attached to the 9-position of the purine and to the 1-position of the pyrazolo[3,4-  
13                  d]pyrimidine groups;

14                  Y is a functional linking group selected from a group consisting of -O-, -S-, -NR'-,  
15                  -NH-CO-, trifluoroacetamido and [phtalimido] phthalimido groups where R' is H  
16                  or C<sub>1-6</sub> alkyl, and at least one of the (CH<sub>2</sub>)<sub>m</sub> and (CH<sub>2</sub>)<sub>q</sub> groups is directly linked to  
17                  the -O-, -S-, -NR'-, NH-CO-, trifluoroacetamido and [phtalimido] phthalimido  
18                  groups and the other of said (CH<sub>2</sub>)<sub>m</sub> and (CH<sub>2</sub>)<sub>q</sub> groups is linked to the heterocyclic  
19                  base with a carbon to carbon bond;

20                  m is 1 to 8, inclusive;

21                  q is 0 to 8, inclusive;

22                  r is 0 or 1; and

23                  A' is a group selected from chloro, bromo, iodo, SO<sub>2</sub>R'', S<sup>+</sup>R''R''' and a radical  
24                  which activates the carbon to which it is attached for nucleophilic substitution,  
25                  where each of R'' and R''' is independently C<sub>1-6</sub> alkyl or aryl or R'' and R'''  
26                  together form a C<sub>1-6</sub> alkylene bridge.

1                   2. An oligonucleotide according to claim 1 wherein B is selected from  
2                  adenine-8-yl, guanine-8-yl, 4-aminopyrazolo[3,4-d]pyrimidin-3-yl, and 4-amino-6-  
3                  oxopyrazolo[3,4-d]pyrimidin-3-yl groups.

1                   3. An oligonucleotide according to claim 1 wherein m is 1, 2 or 3; q is  
2                  2, 3, or 4; and r is 1.

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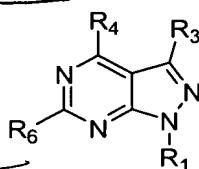
1                   4. An oligonucleotide according to claim 1 wherein the R<sub>1</sub> group is 1-  
2                    (β-D-ribofuranosyl).

1                   5. An oligonucleotide according to claim 1 wherein the R<sub>1</sub> group is 1-  
2                    (β-D-2-deoxyribofuranosyl).

1                   6. An oligonucleotide according to claim 1 wherein the R<sub>1</sub> group is 1-  
2                    (β-D-2-O-methyl-ribofuranosyl).

1                   7. An oligonucleotide according to claim 1 wherein the group  
2                    -(CH<sub>2</sub>)<sub>q</sub>-(Y)<sub>r</sub>-(CH<sub>2</sub>)<sub>m</sub>-A' is 3-iodoacetamidopropyl, 3-(4-bromobutyramido)propyl, 4-  
3                    iodoacetamidobutyl, or 4-(4-bromobutyramido)butyl.

8. (Amended) A compound of the formula



3                   where R<sub>1</sub> is H, or a 1-(β-D-ribofuranosyl) or 1-(β-D-deoxyribofuranosyl) group which  
4                    is optionally substituted on one or more of its hydroxyl functions with a Z group  
5                    wherein Z independently is methyl or a phosphate, thiophosphate, alkylphosphate  
6                    or alkanephosphonate group, or a reactive precursor of said phosphate,  
7                    thiophosphate, alkylphosphate or alkanephosphonate group which precursor is  
8                    suitable for internucleotide bond formation;

9. 42 R<sub>3</sub> is (CH<sub>2</sub>)<sub>q</sub>-(Y)<sub>r</sub>-(CH<sub>2</sub>)<sub>m</sub>-A" where A" is a group selected from chloro, bromo, iodo,  
10                   SO<sub>2</sub>R", S<sup>+</sup>R"R"" and a radical which activates the carbon to which it is attached  
11                   for nucleophilic substitution, where each of R" and R"" is independently C<sub>1-6</sub>  
12                   alkyl or aryl or R" and R"" together form a C<sub>1-6</sub> alkylene bridge, or A" is an  
13                   intercalator group, a metal ion chelator or a reporter group;

14                   Y is a functional linking group selected from a group consisting of -O-, -S-, -NR'-,  
15                   -NH-CO-, trifluoroacetamido and [phtalimido] phthalimido groups where R' is H  
16                   or C<sub>1-6</sub> alkyl, and at least one of the (CH<sub>2</sub>)<sub>m</sub> and (CH<sub>2</sub>)<sub>q</sub> groups is directly linked to  
17                   said -O-, -S-, -NR'-, NH-CO-, trifluoroacetamido and [phtalimido] phthalimido  
18                   groups and the other of said (CH<sub>2</sub>)<sub>m</sub> and (CH<sub>2</sub>)<sub>q</sub> groups is linked to the heterocyclic  
19                   base with a carbon to carbon bond;

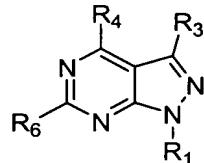
(35)

20 each of m and q is independently 0 to 8, inclusive; r is 0 or 1 provided that when A" is  
21 a group selected from chloro, bromo, iodo,  $\text{SO}_2\text{R}''$ ,  $\text{S}^+\text{R}''\text{R}'''$  and a radical which  
22 activates the carbon to which it is attached for nucleophilic substitution, then m is  
23 not 0;  
24 each of  $\text{R}_4$  and  $\text{R}_6$  is independently H, OR, SR, NHOR,  $\text{NH}_2$ , or  $\text{NH}(\text{CH}_2)_t\text{NH}_2$  where  
25 R is H or  $\text{C}_{1-6}$ alkyl and t is an integer from 0 to 12.

1 9. A compound in accordance with claim 8 where each of  $\text{R}_4$  and  $\text{R}_6$   
2 is independently selected from a group consisting of H, OH and  $\text{NH}_2$ .

1 10. A compound of the formula

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3 where  $\text{R}_1$  is H, or a 1-( $\beta$ -D-ribofuranosyl) or 1-( $\beta$ -D-deoxyribofuranosyl) group which  
4 is optionally substituted on one or more of its hydroxyl functions with a Z group  
5 wherein Z independently is methyl or a phosphate, thiophosphate, alkylphosphate  
6 or alkanephosphonate group, or a reactive precursor of said phosphate,  
7 thiophosphate, alkylphosphate or alkanephosphonate group which precursor is  
8 suitable for internucleotide bond formation;

9  $\text{R}_3$  is  $(\text{CH}_2)_q-(\text{Y})-(\text{CH}_2)_m-\text{A}''$  where  $\text{A}''$  is a reporter group;

10 Y is a functional linking group selected from a group consisting of -O-, -S-, -NR'-,  
11 -NH-CO-, trifluoroacetamido and [phtalimido] phtalimido groups where R' is H  
12 or  $\text{C}_{1-6}$  alkyl, and at least one of the  $(\text{CH}_2)_m$  and  $(\text{CH}_2)_q$  groups is directly linked to  
13 said -O-, -S-, -NR'-, NH-CO-, trifluoroacetamido and [phtalimido] phtalimido  
14 groups and the other of said  $(\text{CH}_2)_m$  and  $(\text{CH}_2)_q$  groups is linked to the heterocyclic  
15 base with a carbon to carbon bond;

16 each of m and q is independently 0 to 8, inclusive; r is 0 or 1, and

17 each of  $\text{R}_4$  and  $\text{R}_6$  is independently H, OR, SR, NHOR,  $\text{NH}_2$ , or  $\text{NH}(\text{CH}_2)_t\text{NH}_2$  where  
18 R is H or  $\text{C}_{1-6}$ alkyl and t is an integer from 0 to 12.

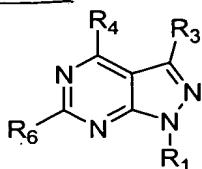
1 11. A compound in accordance with claim 10 where each of  $\text{R}_4$  and  $\text{R}_6$   
2 is independently selected from a group consisting of H, OH and  $\text{NH}_2$ .

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1 12. A compound in accordance with claim 11 where the reporter group  
2 is biotin or 2,4-dinitrobenzene.

1 13. An oligonucleotide having at least one nucleotide of the formula

1 T, 3157



2 where R<sub>1</sub> is a 1-(β-D-ribofuranosyl) or 1-(β-D-2-deoxyribofuranosyl) group which is  
3 optionally substituted on one or more of its hydroxyl functions with a Z group  
4 wherein Z independently is methyl or a phosphate, thiophosphate, alkylphosphate  
5 or alkanephosphonate group;

6 R<sub>3</sub> is (CH<sub>2</sub>)<sub>q</sub>-(Y)<sub>r</sub>-(CH<sub>2</sub>)<sub>m</sub>-A and A is a reporter group;

7 Y is a functional linking group selected from a group consisting of -O-, -S-, -NR'-,  
8 -NH-CO-, trifluoroacetamido and [phtalimido] phthalimido groups where R' is H  
9 or C<sub>1-6</sub> alkyl, and at least one of the (CH<sub>2</sub>)<sub>m</sub> and (CH<sub>2</sub>)<sub>q</sub> groups is directly linked to  
10 said -O-, -S-, -NR'-, NH-CO-, trifluoroacetamido and [phtalimido] phthalimido  
11 groups and the other of said (CH<sub>2</sub>)<sub>m</sub> and (CH<sub>2</sub>)<sub>q</sub> groups is linked to the heterocyclic  
12 base with a carbon to carbon bond;

13 each of m and q is independently 0 to 8, inclusive; r is 0 or 1, and

14 each of R<sub>4</sub> and R<sub>6</sub> is independently H, OR, SR, NHOR, NH<sub>2</sub>, or NH(CH<sub>2</sub>)<sub>n</sub>NH<sub>2</sub> where  
15 R is H or C<sub>1-6</sub>alkyl and t is an integer from 0 to 12.

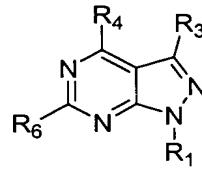
1 14. An oligonucleotide in accordance with claim 13 where each of R<sub>4</sub>  
2 and R<sub>6</sub> is independently selected from a group consisting of H, OH and NH<sub>2</sub>.

1 15. An oligonucleotide in accordance with claim 14 where the reporter  
2 group is biotin or 2,4-dinitrobenzene.

1 T

1 16. (New) A compound having the formula

1 T, 3157



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2 cont'd.

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3 5 wherein R<sub>1</sub> is H, or a 1-( $\beta$ -D-ribofuranosyl) or 1-( $\beta$ -D-2-deoxyribofuranosyl) group  
4 which is optionally substituted on one or more of its hydroxyl functions with a Z  
5 group wherein Z independently is methyl or a phosphate, thiophosphate,  
6 alkylphosphate or alkanephosphonate group which precursor is suitable for  
7 internucleotide bond formation;

8 R<sub>3</sub> is -W-X, wherein W is a chemical linker arm selected from the group consisting of  
9 C<sub>1-12</sub> alkylene, C<sub>2-12</sub> alkenylene and C<sub>2-12</sub> alkynylene, and X is selected from the  
10 group consisting of OH, SH, NH<sub>2</sub> and chemically blocked derivatives thereof;  
11 each of R<sub>4</sub> and R<sub>6</sub> is independently H, OR, SR, NHOR, NH<sub>2</sub>, or NH(CH<sub>2</sub>)<sub>t</sub>NH<sub>2</sub> where  
12 R is H or C<sub>1-6</sub>alkyl and t is an integer from 0 to 12  
13 with the proviso that when W is -CH<sub>2</sub>CH<sub>2</sub>-, then X is other than NH<sub>2</sub>.

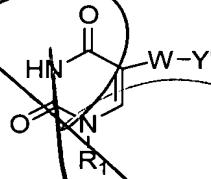
1 17. (New) A compound of claim 16, wherein W is C<sub>1-12</sub> alkylene and  
2 X is selected from the group consisting of OH, NH<sub>2</sub> and chemically blocked derivatives  
3 thereof.

1 18. (New) A compound of claim 16, wherein W is C<sub>2-12</sub> alkynylene  
2 and X is selected from the group consisting of OH, NH<sub>2</sub> and chemically blocked  
3 derivatives thereof.

1 19. (New) A compound of claim 17, wherein W is pentyl and X is  
2 NH-trityl.

1 20. (New) A compound of claim 16, wherein R<sub>4</sub> is NH<sub>2</sub> or OH and R<sub>6</sub>  
2 is H or NH<sub>2</sub>

1 21. (New) A compound having the formula

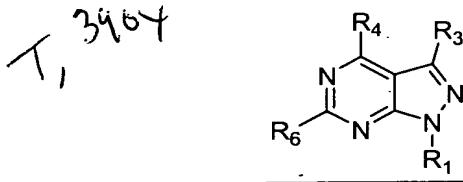


3 wherein R<sub>1</sub> is a 1-( $\beta$ -D-ribofuranosyl) or 1-( $\beta$ -D-2-deoxyribofuranosyl) group which  
4 is optionally substituted on one or more of its hydroxyl functions with a Z group  
5 wherein Z independently is methyl or a phosphate, thiophosphate, alkylphosphate  
6 or alkanephosphonate group which precursor is suitable for internucleotide bond  
7 formation:

8 W is a chemical linker arm selected from the group consisting of C<sub>2-12</sub> alkynylene,  
9 and Y' is selected from the group consisting of OH, SH and chemically blocked  
10 derivatives thereof.

1 22. (New) A compound of claim 21, wherein Y' is selected from the  
2 group consisting of OH and chemically blocked derivatives thereof.

1 I 21 23. (New) An oligonucleotide comprising at least one nucleotide unit  
2 of the formula



4 wherein R<sub>1</sub> is a 1-(β-D-ribofuranosyl) or 1-(β-D-2-deoxyribofuranosyl) group which  
5 is optionally substituted on one or more of its hydroxyl functions with a Z group  
6 wherein Z independently is methyl or a phosphate, thiophosphate, alkylphosphate  
7 or alkanephosphonate group which precursor is suitable for internucleotide bond  
8 formation;

9 R<sub>3</sub> is -W-X, wherein W is a chemical linker arm selected from the group consisting of  
10 C<sub>1-12</sub> alkylene, C<sub>2-12</sub> alkenylene and C<sub>2-12</sub> alkynylene, and X is selected from the  
11 group consisting of OH, SH, NH<sub>2</sub> and chemically blocked derivatives thereof;  
12 each of R<sub>4</sub> and R<sub>6</sub> is independently H, OR, SR, NHOR, NH<sub>2</sub>, or NH(CH<sub>2</sub>)<sub>t</sub>NH<sub>2</sub> where  
13 R is H or C<sub>1-6</sub>alkyl and t is an integer from 0 to 12.

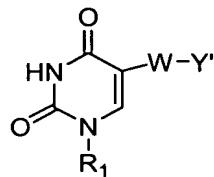
1 22 24. (New) An oligonucleotide of claim 23, wherein W is C<sub>1-12</sub>  
2 alkylene and X is selected from the group consisting of OH, NH<sub>2</sub> and chemically blocked  
3 derivatives thereof.

1 23 25. (New) An oligonucleotide of claim 23, wherein W is C<sub>2-12</sub>  
2 alkynylene and X is selected from the group consisting of OH, NH<sub>2</sub> and chemically  
3 blocked derivatives thereof.

1 24 26. (New) An oligonucleotide of claim 24, wherein W is pentyl and X  
2 is NH-trityl.

1  
2 of the formula

27. (New) An oligonucleotide comprising at least one nucleotide unit



4 1 wherein R<sub>1</sub> is a 1-( $\beta$ -D-ribofuranosyl) or 1-( $\beta$ -D-2-deoxyribofuranosyl) group which  
5 is optionally substituted on one or more of its hydroxyl functions with a Z group  
6 wherein Z independently is methyl or a phosphate, thiophosphate, alkylphosphate  
7 or alkanephosphonate group which precursor is suitable for internucleotide bond  
8 formation;

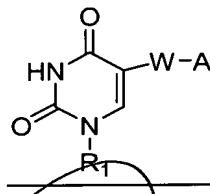
9 R<sub>3</sub> is  $-W-A$ , wherein W is a chemical linker arm selected from the group consisting of  
10 C<sub>1-12</sub> alkylene, C<sub>2-12</sub> alkenylene and C<sub>2-12</sub> alkynylene, and A is a reporter group;  
11 and

12 each of R<sub>4</sub> and R<sub>6</sub> is independently H, OR, SR, NHOR, NH<sub>2</sub>, or NH(CH<sub>2</sub>)<sub>t</sub>NH<sub>2</sub> where  
13 R is H or C<sub>1-6</sub>alkyl and t is an integer from 0 to 12.

1 30 34. (New) A labeled oligonucleotide of claim 33, wherein said  
2 reporter group is selected from the group consisting of <sup>3</sup>H, <sup>125</sup>I, <sup>35</sup>S, <sup>14</sup>C and <sup>32</sup>P.

3 31 35. (New) A labeled oligonucleotide of claim 33, wherein said  
4 reporter group is <sup>3</sup>H.

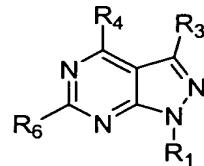
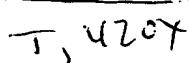
5 36. (New) A labeled oligonucleotide comprising at least one  
6 nucleotide unit of the formula



7 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 157 158 159 160 161 162 163 164 165 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200 201 202 203 204 205 206 207 208 209 210 211 212 213 214 215 216 217 218 219 220 221 222 223 224 225 226 227 228 229 230 231 232 233 234 235 236 237 238 239 240 241 242 243 244 245 246 247 248 249 250 251 252 253 254 255 256 257 258 259 260 261 262 263 264 265 266 267 268 269 270 271 272 273 274 275 276 277 278 279 280 281 282 283 284 285 286 287 288 289 290 291 292 293 294 295 296 297 298 299 300 301 302 303 304 305 306 307 308 309 310 311 312 313 314 315 316 317 318 319 320 321 322 323 324 325 326 327 328 329 330 331 332 333 334 335 336 337 338 339 340 341 342 343 344 345 346 347 348 349 350 351 352 353 354 355 356 357 358 359 360 361 362 363 364 365 366 367 368 369 370 371 372 373 374 375 376 377 378 379 380 381 382 383 384 385 386 387 388 389 390 391 392 393 394 395 396 397 398 399 400 401 402 403 404 405 406 407 408 409 410 411 412 413 414 415 416 417 418 419 420 421 422 423 424 425 426 427 428 429 430 431 432 433 434 435 436 437 438 439 440 441 442 443 444 445 446 447 448 449 450 451 452 453 454 455 456 457 458 459 460 461 462 463 464 465 466 467 468 469 470 471 472 473 474 475 476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 491 492 493 494 495 496 497 498 499 500 501 502 503 504 505 506 507 508 509 510 511 512 513 514 515 516 517 518 519 520 521 522 523 524 525 526 527 528 529 530 531 532 533 534 535 536 537 538 539 540 541 542 543 544 545 546 547 548 549 550 551 552 553 554 555 556 557 558 559 560 561 562 563 564 565 566 567 568 569 570 571 572 573 574 575 576 577 578 579 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 595 596 597 598 599 600 601 602 603 604 605 606 607 608 609 610 611 612 613 614 615 616 617 618 619 620 621 622 623 624 625 626 627 628 629 630 631 632 633 634 635 636 637 638 639 640 641 642 643 644 645 646 647 648 649 650 651 652 653 654 655 656 657 658 659 660 661 662 663 664 665 666 667 668 669 670 671 672 673 674 675 676 677 678 679 680 681 682 683 684 685 686 687 688 689 690 691 692 693 694 695 696 697 698 699 700 701 702 703 704 705 706 707 708 709 710 711 712 713 714 715 716 717 718 719 720 721 722 723 724 725 726 727 728 729 730 731 732 733 734 735 736 737 738 739 740 741 742 743 744 745 746 747 748 749 750 751 752 753 754 755 756 757 758 759 760 761 762 763 764 765 766 767 768 769 770 771 772 773 774 775 776 777 778 779 780 781 782 783 784 785 786 787 788 789 790 791 792 793 794 795 796 797 798 799 800 801 802 803 804 805 806 807 808 809 810 811 812 813 814 815 816 817 818 819 820 821 822 823 824 825 826 827 828 829 830 831 832 833 834 835 836 837 838 839 840 841 842 843 844 845 846 847 848 849 850 851 852 853 854 855 856 857 858 859 860 861 862 863 864 865 866 867 868 869 870 871 872 873 874 875 876 877 878 879 880 881 882 883 884 885 886 887 888 889 890 891 892 893 894 895 896 897 898 899 900 901 902 903 904 905 906 907 908 909 910 911 912 913 914 915 916 917 918 919 920 921 922 923 924 925 926 927 928 929 930 931 932 933 934 935 936 937 938 939 940 941 942 943 944 945 946 947 948 949 950 951 952 953 954 955 956 957 958 959 960 961 962 963 964 965 966 967 968 969 970 971 972 973 974 975 976 977 978 979 980 981 982 983 984 985 986 987 988 989 990 991 992 993 994 995 996 997 998 999 1000 1001 1002 1003 1004 1005 1006 1007 1008 1009 1010 1011 1012 1013 1014 1015 1016 1017 1018 1019 1020 1021 1022 1023 1024 1025 1026 1027 1028 1029 1030 1031 1032 1033 1034 1035 1036 1037 1038 1039 1040 1041 1042 1043 1044 1045 1046 1047 1048 1049 1050 1051 1052 1053 1054 1055 1056 1057 1058 1059 1060 1061 1062 1063 1064 1065 1066 1067 1068 1069 1070 1071 1072 1073 1074 1075 1076 1077 1078 1079 1080 1081 1082 1083 1084 1085 1086 1087 1088 1089 1090 1091 1092 1093 1094 1095 1096 1097 1098 1099 1100 1101 1102 1103 1104 1105 1106 1107 1108 1109 1110 1111 1112 1113 1114 1115 1116 1117 1118 1119 1120 1121 1122 1123 1124 1125 1126 1127 1128 1129 1130 1131 1132 1133 1134 1135 1136 1137 1138 1139 1140 1141 1142 1143 1144 1145 1146 1147 1148 1149 1150 1151 1152 1153 1154 1155 1156 <u

38. (New) A labeled oligonucleotide of claim 36, wherein said reporter group is  $^3\text{H}$ .

~~T 32~~ 39. (New) A compound having the formula



wherein R<sub>1</sub> is H, or a 1-( $\beta$ -D-ribofuranosyl) or 1-( $\beta$ -D-2-deoxyribofuranosyl) group which is optionally substituted on one or more of its hydroxyl functions with a Z group wherein Z independently is methyl or a phosphate, thiophosphate, alkylphosphate or alkanephosphonate group which precursor is suitable for internucleotide bond formation;

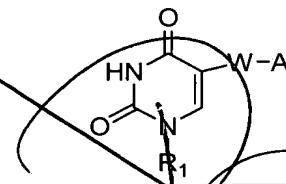
R<sub>3</sub> is -W-A, wherein W is a chemical linker arm selected from the group consisting of C<sub>1-12</sub> alkylene, C<sub>2-12</sub> alkenylene and C<sub>2-12</sub> alkynylene, and A is a reporter group; and

each of R<sub>4</sub> and R<sub>6</sub> is independently H, OR, SR, NHOR, NH<sub>2</sub>, or NH(CH<sub>2</sub>)<sub>t</sub>NH<sub>2</sub> where R is H or C<sub>1-6</sub>alkyl and t is an integer from 0 to 12.

40. (New) A compound of claim 39, wherein said reporter group is selected from the group consisting of  $^3\text{H}$ ,  $^{125}\text{I}$ ,  $^{35}\text{S}$ ,  $^{14}\text{C}$  and  $^{32}\text{P}$ .

41. (New) A compound of claim 39, wherein said reporter group is  $^3\text{H}$ .

42. (New) A compound having the formula



wherein  $R_1$  is a 1-( $\beta$ -D-ribofuranosyl) or 1-( $\beta$ -D-2-deoxyribofuranosyl) group which is optionally substituted on one or more of its hydroxyl functions with a  $Z$  group wherein  $Z$  independently is methyl or a phosphate, thiophosphate, alkylphosphate or alkanephosphonate group which precursor is suitable for internucleotide bond formation;

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8       W is a chemical linker arm selected from the group consisting of C<sub>2-12</sub> alkynylene;  
9               and  
10       A is a reporter group.

1       43. (New) A compound of claim 42, wherein said reporter group is  
2       selected from the group consisting of <sup>3</sup>H, <sup>125</sup>I, <sup>35</sup>S, <sup>14</sup>C and <sup>32</sup>P.

1       44. (New) A compound of claim 42, wherein said reporter group is <sup>3</sup>H.

*G3*  
*(uncl'd)*  
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